REMARKS

Claims 126, 128, 144 and 149 are amended; claims 1-125, 129-130, 132-143, 145-148, 151-156, and 158 are canceled; claims 160-164 are added. Upon entry of the present amendment, claims 126, 127, 128, 131, 144, 149, 150, 157, 159 and 160-164 are pending.

Support for the amendments is found in the application and claims as originally filed. For example, support for claim 128, which recites "by detecting growth of bacterial cells in the sample" is provided at page 52, lines 9-24, under the header "RP-factor activity." Support for new claims 160-164 is found at claims 126, 128, and 144. No new matter has been added.

Objection to the Claims

The objection to claims 126 and 144 is overcome by the present amendment.

Objection to the Specification

The Examiner objects to the specification based on the assertion that Applicants' specification fails to provide support for polypeptides having 95% identity to SEQ ID NO. 2. Applicants respectfully disagree.

Contrary to the Examiner's assertions, Applicants' specification is not limited to the purified RP factor described in the Examples. Applicants' specification clearly states describes the use of polypeptides having at least 95% identity to RP factor (SEQ ID NO:2), which sequence is described at Figure 1. More specifically, at page 23, lines 5-9, Applicants' specification states:

> Particularly preferred are homologues, derivatives, muteins or equivalents of the RP-factor of the invention which have at least 30% homology, for example at least 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 95% homology with any one of the particular amino acid sequences shown in Fig. 1A or Fig. 1B (emphasis added).

In view of this disclosure, Applicants' specification clearly encompasses the use of RP-factors having at least 95% identity to SEQ ID No. 2. Therefore, this objection to the specification should be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

The rejection of claim 159 as allegedly indefinite is rendered moot by the cancellation of the claim.

The rejection of claims 128, 144, and 158 is overcome by the present amendment.

Rejections under 35 U.S.C. § 112, first paragraph

New Matter

Claims 126-128, 131, 144, 148-150, and 157-159 are rejected under 35 U.S.C. § 112, first paragraph as allegedly including new matter that was not described in the application as filed. In support of the rejection, the Examiner asserts that the specification fails to provide support for polypeptides having at least 95% sequence identity to SEQ ID NO:2 or to amino acids 117-184 of SEQ ID NO:2. This is incorrect.

Figure 1A provides the sequence of a number of RP factors, including SEQ ID NO:2 and the asterisks in Figure 1A identify amino acids 117-184 of SEQ ID NO:2. As detailed above, Applicants' specification describes such sequences at page 23, lines 5-9:

> Particularly preferred are homologues, derivatives, muteins or equivalents of the RP-factor of the invention which have at least 30% homology, for example at least 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% homology with any one of the particular amino acid sequences shown in Fig. 1A or Fig. 1B (emphasis added).

In view of this disclosure, the new matter rejection is improper and should be withdrawn.

Written Description

Claims 126-128, 131, 144, 148-150, and 157-159 are further rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking a written description. In support of the rejection, the Examiner indicates that Applicants have not described a sufficient number of polypeptide variants to establish how sequence changes would affect the function of the protein. Applicants respectfully disagree.

An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the Applicants had possession of the claimed invention (M.P.E.P. 2163.04 II.A.3(a)). Applicants' specification clearly satisfies the written description requirement. Using sequence information relating to *M. luteus* RP-factor, Applicants have identified RP factor proteins from other bacteria, including SEQ ID NO:2 from *M. tuberculosis*, that share sequence identity with *M. luteus* RP-factor (page 34, line 21, to page 35, line 3, under the header "Identification of RP-factor homologues"), and Applicants have used this information to identify conserved structural features. Specifically, Applicants have identified two RP-factors from *M. luteus* and one from *M. tuberculosis* (Figure 1A; page 34, line 21, to page 35, line 4).

In addition, Applicants have identified RP-factors from *M. leprae* and *Streptomyces coelicolor*, *Streptomyces rimosus, Mycobacterium smegmatis,* which includes four similar genes, *Mycobacterium bovis,* and *Cornebacterium glutamicum,* which includes two similar genes (Figure 1A; page 34, line 21, to page 35, line 4). Applicants have provided an alignment of RP factor proteins in Figure 1A, which identifies conserved structural features and highly conserved amino acid residues (page 35, lines 5-34; Figures 9A and 9B). Applicants found that RP-factors share a secretory signal sequence and a conserved 70-residue segment that may act as a signaling domain (page 35, lines 5-18, under the heading "Domain structure"). This domain includes four conserved tryptophan residues and two conserved cysteine residues that may form a disulfide bridge (page 35, lines 25-30). These structural features are conserved among a wide variety of proteins and are, therefore, likely to be functionally important. Accordingly, Applicants' specification provides guidance relating to those regions of the protein where sequence

variations are likely to be tolerated and those conserved regions where variations in the sequence are less desirable.

Moreover, one of skill in the art could readily identify those variant polypeptides that fall within the scope of Applicants' claims (i.e., those polypeptides having at least 95% amino acid sequence identity to SEQ ID NO:2 that are capable of resuscitating a dormant, moribund, or latent *Mycobacterium tuberculosis* cell) using routine methods that are described in Applicants' specification. For example, Applicants' specification clearly describes methods of screening for polypeptides capable of resuscitating dormant bacteria using purified RP-factors (page 33, line 20, to page 34, line 3, page 35, lines 35-44). Such screening could easily be accomplished using standard techniques that are plainly described in Applicants' specification.

In particular, Applicants expressed a secreted form of the *M. tuberculosis* polypeptide in *E. coli* (page 38, line 31 to page 39, line 10). This fragment of SEQ ID NO:2 included amino acids beginning at D50 of the amino acid sequence, and included amino acids 117-184 as recited in the claims (page 39, lines 11-15). The purified protein was added to cultures of *M. luteus* and *M. tuberculosis*. Applicants found that as expected SEQ ID NO:2 stimulated the growth of *M. tuberculosis* cells and *M. luteus* cells (page 39, lines 24-34, under the header "Effect of *M. luteus* RP-factor on growth of *Mycobacterium tuberculosis* cells isolated from macrophages"). This growth stimulation occurred under conditions where a control culture had ceased to grow (page 39, lines 19-22). Applicants found that the control culture grew to a final OD_{600nm} of 1.0 (page 39, lines 19-22). In contrast, cultures treated with purified RP-factor continued to grow to final OD_{600nm} of 2.0-6.0 (page 39, lines 20-22). These results indicated that a SEQ ID NO:2 polypeptide containing amino acids 117-184 was capable of resuscitating a dormant, moribund, or latent *Mycobacterium tuberculosis* cell under conditions where the control culture failed to grow.

In sum, Applicants have described a number of polypeptide variants, have described a correlation between structure and function, and have described methods for identifying polypeptides having the desired biological activity. This description clearly establishes that Applicants had possession of the invention as claimed. Accordingly, the written description rejection should be withdrawn.

New Claims

Applicants have added new claims 160-164, which are directed to methods for resuscitating dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells that feature the use of a polypeptide comprising SEQ ID NO: 2 or comprising at least amino acid residues 117 to 184 of SEQ ID NO: 2. In particular, claims 160 and 161 are directed to methods of resuscitating a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell by contacting the *Mycobacterium tuberculosis* bacterial cell *in vitro* with a purified polypeptide comprising SEQ ID NO:2 (claim 160) or a purified polypeptide comprising at least amino acid residues 117 to 184 of SEQ ID NO: 2 (claim 161), where the polypeptide is capable of resuscitating a dormant, moribund, or latent *Mycobacterium tuberculosis* cell; and incubating the bacterial cells in culture medium containing the polypeptide, thereby resuscitating said bacterial cells. Claim 162 depends from claims 160 and 161.

Claims 163 and 164 are directed to methods of resuscitating dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells by contacting the bacterial cells *in vitro* with a cell strain expressing a nucleic acid encoding a polypeptide comprising SEQ ID NO: 2 (claim 163) or encoding at least amino acid residues 117 to 184 of SEQ ID NO: 2, where the polypeptide is capable of resuscitating a dormant, moribund, or latent *Mycobacterium tuberculosis* cell; and incubating the cells and cell strain in culture medium, thereby resuscitating the cells.

Applicants believe that these claims are commensurate in scope with the subject matter that the Examiner has indicated is allowable. Accordingly, allowance of claims 160-164 is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe the pending application as amended herein is in condition for allowance. Therefore, Applicants respectfully request entry of the amendments and remarks presented herein, favorable reconsideration and withdrawal of all pending rejections, and issuance of a Notice of Allowance. However, if the Examiner disagrees and a telephone conference would be helpful to expedite further prosecution and allowance of this application, Applicants respectfully request the Examiner to contact the undersigned at the telephone number indicated below.

Dated: May 5, 2010

Respectfully submitted,

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